INF2178 (Winter 2024)
Michelle Lee (#1001448169)

Introduction

In recent decades, the introduction of MRI technology has significantly improved medical practitioners' understanding of neurodegenerative diseases, particularly dementia, which poses profound challenges to healthcare systems worldwide. This study aims to explore the complex dynamics of brain volume changes in dementia patients over time using a dataset studying patients with dementia diagnosis and their MRI results. We will assess the patterns of brain atrophy and their association with the diagnosis of dementia and cognitive decline. By applying mixed-effects ANOVA, we aim to statistically examine the effects of different variables in the dataset including brain volume and its association across hospital visits, the progression of dementia, and cognitive metrics such as the Mini-Mental State Examination (MMSE) scores.

Our goal is to evaluate the trajectory of brain changes in dementia, focusing on the following research questions:

Q: How does brain volume change over multiple visits for people diagnosed with dementia compared to those without a dementia diagnosis?
Q: Is there a statistically significant impact (interaction effect) between the timing of the visits and dementia status on brain volume?
Q: Is the rate of brain volume change consistent across different patient groups throughout the observation period?

Exploratory Data Analysis

This section will help examine, summarize, and visualize the main characteristics of our dataset.

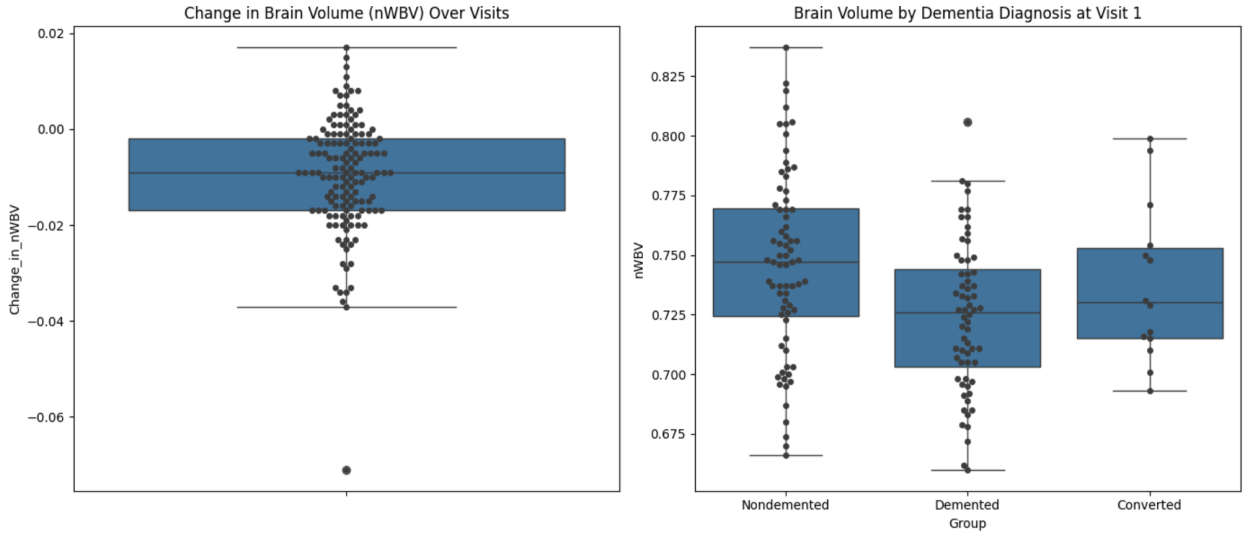

Figure 1 (left): Boxplots for Brain Volume over Visits & **Figure 2** (right) Brain Volume by Dementia Diagnosis

The boxplots above help to visualize overall characteristics of the distribution of data in our dataset. **Figure 1** - which changes in Brain Volume (nWBV) over Visits - shows that distribution of changes in brain volume is centered around zero, indicating no significant increase or decrease in nWBV on average across all patients from Visit 1 to Visit 2. Examining the IQR shows that the range of changes in brain volume spans from slight increases to moderate decreases, with most data points falling within a relatively narrow IQR, suggesting that for most patients, the change in brain volume was relatively minor. We should note however that the presence of outliers, as depicted by the individual points outside of the whiskers, suggests that there are some patients who experienced more notable changes in brain volume.

Figure 2 displays Brain Volume by Dementia Diagnosis at Visit 1. Patients without dementia

(Nondemented) appear to have a higher median nWBV compared to those diagnosed with dementia or those who converted, which may imply a link between higher brain volumes and the absence of dementia symptoms. Meanwhile, the "Converted" group - which represents patients who converted to dementia - displays a wide IQR and a lower median nWBV compared to the nondemented group, but still similar to the demented group. This means that a potential decrease in brain volume associated with the conversion to dementia occurred.

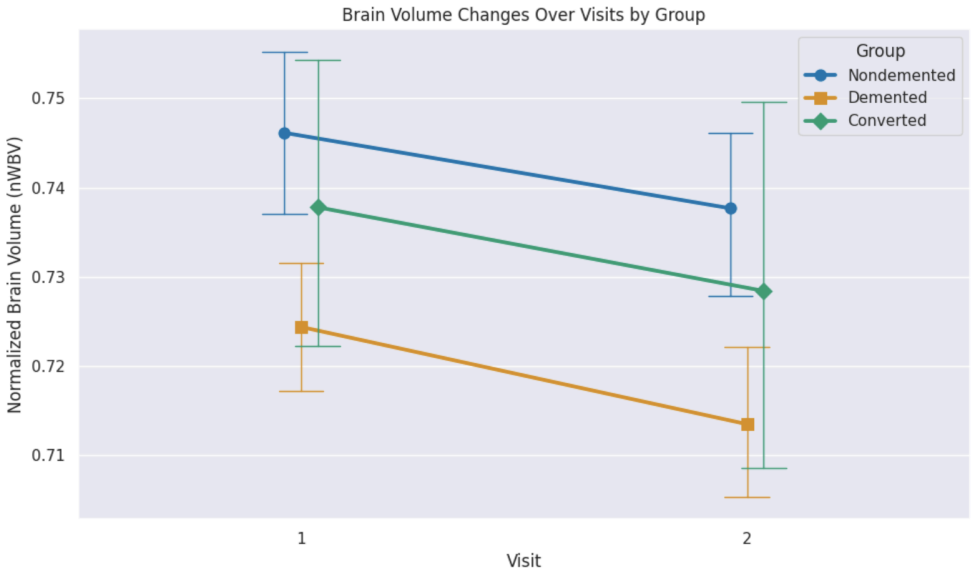

Figure 3: Brain Volume Changes over visits by group

Figure 3 shows there is a decrease in nWBV from Visit 1 to Visit 2 for all patient groups.The ‘nondemented’ group shows the smallest decrease in nWBV and maintains the highest brain volume at both visits compared to the other groups. Meanwhile, the ‘demented’ group shows a larger decrease and overall lower nWBV at both visits than the nondemented group. The ‘converted’ group, which represents individuals who converted from nondemented to demented status between visits, shows the most significant decrease in nWBV and ends with the lowest brain volume at Visit 2.

Power Analysis

Figure 4: Power of Test for effect size = 0.7

The above plot helps to understand the impact of different effect sizes on the power of the test. According to power analysis via Statsmodels on Python, the sample size needed for our experimental setup given: power = 0.91, alpha = 0.05, and effect size = 0.7 is 45.451.

Results

Mixed Effects ANOVA

Source	Sum of Squares	Degrees of Freedom (Effect)	Degrees of Freedom (Error)	Mean Square	F-Value	P-Value (uncorrected)	Partial Eta Squared (Measure of effect size)	Epsilon
Group	0.034	2	141	0.017	6.712	0.002	0.087	-
Visit	0.007	1	141	0.007	94.251	0.000	0.401	1.000
Interaction	0.000	2	141	0.000	1.534	0.219	0.021	-

From the results above, while there are differences in brain volume between groups over time, the pattern of change over this period does not differ significantly between our patient groups. For instance, the Epsilon value for the interaction effect is 'NaN', which could mean due to a lack of variation in the data for that interaction or a small sample size for one of the groups, there wasn't a proper value to perform calculations with. In addition, there is also a statistically significant difference between patient groups ($p = 0.002$), with a moderate effect size (partial eta squared = 0.087). This indicates some differences in average brain volume between the groups. For visit factor (within-subjects), our results suggest some relative significant brain volume patients across the visits ($p < 0.001$), with a large effect size (partial eta squared = 0.401). This indicates that brain volume changes somewhat significantly from one visit to another for patients. However, the interaction effect between the group and visit is not statistically significant ($p = 0.219$), with a very small effect size (partial eta squared = 0.021). This means that the change in brain volume over the visits does not statistically differ too significantly overall.

Post-Hoc Analysis

This section will evaluate using statistical tests whether the conditions for ANCOVA were met based on the characteristics of our dataset.

Assumption 1: Homogeneity of Variances - Levene's Test

Levene's Test statistic: 0.5305	**P-Value**: 0.7531

Levene's test is used to check whether the variances of the scores are equal across our selected group variances. From our results, since the p-value 0.7531 is much larger than the typical significance level (0.05), we do not have evidence to reject the null hypothesis. Therefore, the test did not detect a statistically significant difference in variances among the different patient groups and we can assume that the variances are homogeneous across the different groups and visits.

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Assumption 2: Normality of Residuals - Shapiro-Wilk's Test

Group	Visit	Shapiro-Wilk Statistic	P-Value
Non-Demented	1	0.9887	0.7720
	2	0.9839	0.5109
Demented	1	0.9920	0.9546
	2	0.9795	0.3847
Converted	1	0.9335	0.3415
	2	0.9403	0.5024

Shapiro-Wilk's test is used to check the normality of the residuals. Based on results above, since our grouped patient's p-values are greater than 0.05 - this overall suggests that the data does not significantly deviate from a normal distribution. Therefore, we fail to reject the null hypothesis and this indicates that there is no evidence to suggest the data is not normally distributed. We can assume then that the assumption of normality for conducting an ANOVA is met based on results.

Discussion

Our Post-Hoc assumption test results support the validity of the ANOVA results, which revealed significant differences in brain volume between groups and across visits. The significant main effects indicate that both the diagnosis of dementia and the progression of time are associated with changes in brain volume. However, these factors may occur independently of each other, as indicated by the non-significant interaction term. Overall, though multiple testing of assumptions, we have affirmed the reliability of the ANOVA findings through statistically rigorous techniques. These findings conform with existing literature on studies that observe brain volume reduction in individuals with dementia overall. The significant main effect of group status on brain volume (p-value = 0.002) aligns with studies that show brain volumes differ between nondemented and demented status patients. Additionally, the significant main effect of Visit (p-value < 0.001) supports the idea that brain volume decreases over time in the context of dementia. The absence of a significant interaction effect between group status and time means that while both group status and time independently affect brain volume, their combined effect does not differ significantly from what would be expected by looking at each factor separately. This indicates that the rate of brain volume change over the observed period is similar across all groups. Some existing research suggests that those with dementia may experience a *faster* rate of atrophy, such as Welsh et al. (1994). Therefore, the lack of a significant interaction in our own study might be due to other unaccounted for factors in our dataset including sample size, the specific time frame of MRI visits, or the stage of dementia in the participants.

Conclusion

In conclusion, this mixed-effects ANOVA experiment showed that patient groups—nondemented, demented, and converted—have different brain volume profiles over time. While the progression over time affected the patients similarly, the lack of a significant interaction suggests that the trajectory of brain volume change is not dependent on dementia status. Our study emphasizes the significance of long-term imaging studies like MRI for diagnosing the complexities of neurological disorders and highlights the need for additional research into the determinants of brain volume alterations for dementia-prone patients.

References

Welsh, K. A., Hoffman, J. M., Earl, N. L., & Hanson, M. W. (1994). Neural correlates of dementia: regional brain metabolism (FDG-PET) and the CERAD neuropsychological battery. *Archives of Clinical Neuropsychology*, *9*(5), 395-409.